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Snakebite envenomation: A comprehensive evaluation of severity, treatment, and outcomes in 100 patients correlating timing of ASV administration with complications

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Abstract

This study, conducted at the New Civil Hospital in Surat from June 2004 to November 2006, explored the clinical dynamics, complications, and outcomes of 100 cases of poisonous snakebites. The age group most affected was 21–40 years (58%), reflective of heightened outdoor activities. Males, often primary earners, exhibited a higher incidence, while rural areas dominated (75%) due to favorable snake habitats. Notable patterns emerged, such as a significant occurrence of bites between 6:00 p.m. and 5:59 a.m. attributed to nocturnal snake activity and rural sleeping habits. The monsoon season experienced a peak in snakebites (79%) as snakes sought refuge in human habitats. Intriguingly, 45% of patients lacked visible fang marks, challenging their reliability for identifying venomous bites. Neurotoxicity prevailed (54%), with local pain and swelling prominent. Effective treatment resulted in a 90% cure rate, highlighting the significance of early diagnosis. Respiratory failure, hypotension, and combined manifestations indicated poor prognosis, underscoring the critical need for early recognition. Mechanical ventilation notably reduced mortality in neurotoxic cases. Delayed admission correlated with heightened severity, complications, and poorer outcomes, emphasizing the urgency of early intervention. Severity grades 3 and 4 exhibited elevated mortality rates, calling for urgent and meticulous management. The duration of venom in the bloodstream before antivenom administration directly impacted severity and outcomes. Future research avenues include species-specific considerations, antivenom advancements, community education, remote healthcare solutions, and long-term follow-up. Limitations encompass single-center data, incomplete records, temporal constraints, limited species identification, and a need to delve into social and cultural factors influencing snakebites.

Keywords: Snakebites; Envenomation; Treatment; Emergency; Anti snake venom (ASV)

1. Introduction

The deep-seated and potentially intrinsic human emotion of fearing snakes has captivated researchers in experimental psychology and evolution. However, despite this potent emotional response, snakes have not been adequately recognized as potential contributors to human diseases. The valuable scientific knowledge derived from the clinical manifestations of snake envenoming in humans has been overlooked for an extended period.[1] Most snakes tend to steer clear of human interaction by withdrawing or concealing themselves. Numerous species employ defensive mechanisms, such as the rattlesnake's rattle and the cobra's hooding, to deter organisms perceived as threats.[2]

Snakes, generally being predators, typically employ various methods, including constriction, aggressive biting, chewing, or the use of venom (with some exceptions like egg-eating snakes), to subdue their prey. The method of venom delivery

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varies among different major groups of snakes.[2] Venomous snakes have been implicated in more fatalities than the combined toll of all other venomous and poisonous creatures. They inhabit diverse habitats worldwide, excluding Antarctica. The majority of snake bites are attributed to nonvenomous snakes, and clinical observations reveal a relatively small number of cases involving venomous snake bites. Despite this, estimates indicate an annual occurrence of over 2.5 million venomous snake bites, leading to more than 125,000 deaths. Snake bites constitute a significant cause of morbidity and mortality in developing countries, with the highest risk observed among local populations in rural tropical areas. The injected venom can induce both local and systemic reactions in the affected tissue. Clinical manifestations may vary depending on factors such as the snake species, age, depth of the bite, amount of venom injected, and the age, gender, and overall health of the victim.[3]

Snake bites pose a significant global health challenge, with an estimated 5.4 million people bitten annually, leading to 1.8 to 2.7 million cases of envenoming. Tragically, around 81,410 to 137,880 people succumb to snake bites each year, and roughly three times as many individuals experience amputations or suffer from other permanent disabilities due to these incidents. The most vulnerable groups are agricultural workers and children, with children often experiencing more severe effects due to their smaller body mass. Snake bites constitute a neglected public health issue, particularly in tropical and subtropical countries, with a higher prevalence in Africa, Asia, and Latin America. In Asia alone, up to 2 million people face envenomation each year, while Africa witnesses an estimated 435,000 to 580,000 snake bites annually requiring treatment. Envenomation disproportionately affects women, children, and farmers in impoverished rural communities of low- and middle-income countries. The burden is most pronounced in regions where health systems are underdeveloped, and medical resources are scarce. Venomous snake bites can lead to acute medical emergencies, involving severe paralysis that impedes breathing, bleeding disorders that may result in fatal hemorrhage, irreversible kidney failure, and extensive local tissue damage causing permanent disability and limb amputation. Addressing this issue requires urgent attention and resources, particularly in regions where the health infrastructure is weakest. [4]

Table 1 Type of Toxins

-	**Example of toxin**	**Snake**	**Function**
Three finger fold polypeptido toxins	bungarotoxins	*Bungarus spp* (other Elapidae Colubridae)	Paralysis by blocking nicotinic acetylcholine receptors
Angiotensin converting enzyme inhibitors and bradykinin potentiating peptides	-	Viperidae	Hypotension
Acetylcholinesterase	-	Elapidoe	Paralysis by destroying acetylcholine
Anticholinesterase	Fasciculins	*Dendroaspis* spp	Paralysis (with dendrotoxins) by depolarising neuromuscular block
Disintegrin and metalloproteinase (ADAM)	Haemorrhagins (atrolysins, jararhagin) procoagulants (fibrolase, ecarin, Russell's viper venom factor X activator)	Viperidae, Elapidae	Endothelial damage bleeding necrosis
AVIT sequence cysteine rich proteins	Mamba intestinal toxin (prokineticin)	*Dendroaspie polylepis*	Painful gut spasm, hyperalgesia, CNS effects
Cobra venom factor, complement	Cobra venom factor	Elapidoe, Viperidae	Tissue damage
Small basic myotoxic peptides	Crotamine and crotasin	*Crotalus durissus* subspecies (some circumscribed geographical populations)	Muscle necrosis and spasm

Calcium dependent type galactose binding lectins	Rhodocytin	*Calloselasma rhodostoma* (and other *Viperidoe Elapidae)*	Platelet effects
Cysteine-rich secretory proteins	-	*Elapidoe Viperidoe* Colubridge	Smooth muscle inhibition
Cysteine proteinase inhibitors	Cystatin	*Viperidae, Elapidae*	Inhibit metalloproteinases
Endothelins	Sarafotoxins	*Atractaspis spp*	Hypertension myocardial effects
Factor V.factor-Xactivators	-	*Viperidae, Australasian Elapidae*	Coagulopathy
Kallikrein (kininogenase) serine proteases	-	*Viperidor*	Hypotension
Kunitz-type proteinase inhibitors	Dendrotoxins	*Dendroaspis spp (and other Elapidoe)*	Depolarising neuromuscular block (inhibition of circulating serine proteases)
Lamino oxidase	-	All	Apoptosis
Natriuretic peptides	-	*Elapidoe* atrial-type and brain-type Viperidoe C-type	Hypotension
Nerve growth factor	-	Many	Not known
Phospholipases A,	Bungarotoxins	*Bungarus* spp (many phospholipases A in venoms of most snakes)	Paralysis by presynaptic block and destruction of nerve terminals, myotoxicity haemolysis, inflammation necrosis, platelet effects
Vascular endothelial growth factor (VEGF)	VEGF-homologous potent hypotensive factor	Viperidae	Endothelial damage, permeability oedema, hypotension

The toxins found in snake venom have the capacity to elicit a spectrum of clinical effects, varying from mild to fatal, encompassing both local and systemic manifestations, as detailed below.

1.1. Cytotoxicity

Enzymes like hyaluronidase and collagenase, along with proteinases and phospholipases, in snake venom cause local tissue injury and inflammation. This leads to pain, edema, and potential complications such as bullae and dermonecrosis. Snake venom metalloproteinases can damage the extracellular matrix, resulting in various tissue reactions, including destruction and reparative actions. Microvascular damage may cause hemorrhage, skeletal muscle necrosis, blistering, and dermonecrosis. Elevated compartmental tissue pressure or subcutaneous tissue pressure may mimic compartment syndrome symptoms.[5,6,7,8]

1.2. Lymphatic System

Snake envenomation contributes to edema through lymphatic system injury, which also plays a role in the systemic absorption of venom toxins. Some venom components are neutralized in the lymphatics, albeit slowly and incompletely.[9]

1.3. Venom-Induced Consumption Coagulopathy

Procoagulant toxins in snake venoms lead to consumption coagulopathy, depleting clotting cascade factors and causing spontaneous or uncontrolled bleeding. Thrombotic microangiopathy may accompany this, characterized by thrombocytopenia, microangiopathic hemolytic anemia, and acute kidney injury.[10,11]

1.4. Thrombosis

Snake envenomation can result in myocardial infarction, stroke, or other thrombotic effects. Mechanisms include hypovolemia, coronary thrombosis, direct venom effects on cardiomyocytes, decreased oxygen-carrying capacity, vasoconstriction, myocardial necrosis, and microvascular thrombin deposition.[12,13]

1.5. Thrombocytopenia or Altered Platelet Function

Severe envenomation from certain snakes can cause thrombocytopenia, leading to spontaneous or uncontrolled hemorrhage. The mechanisms include platelet aggregation, sequestration, decreased production, and venom-induced platelet dysfunction.[14,2]

1.6. Neurotoxicity

Envenomation from certain snakes, especially elapids, can cause neuromuscular paralysis due to postneuromuscular or preneuromuscular synaptic toxins. This paralysis can progress to airway compromise and respiratory insufficiency. Myotoxicity, cardiotoxicity, and hypotension may also result.[2]

1.7. Myotoxicity, Cardiotoxicity, and Hypotension

Direct venom effects on muscles through myotoxic phospholipase A2 can cause myokymia, rhabdomyolysis, respiratory compromise, and inflammation. Hypotension may develop from various venom components, reflecting hypovolemia or anaphylaxis.[15,2]

1.8. Nephrotoxicity

Snake envenomation can lead to acute kidney injury, progressing to chronic kidney disease or renal failure. Different snake venoms cause nephrotoxicity through direct injury mediated by inflammatory cytokines, resulting in glomerular degeneration and atrophy.[16,2]

1.9. Other Effects

Snake venom can induce systemic effects such as nausea, vomiting, diarrhea, and diaphoresis. Complex regional pain syndrome and anaphylaxis may also occur due to prior sensitization to venom components.[2]

This research article aims to comprehensively evaluate snakebite envenomation, emphasizing the correlation between antivenom timing and complications. Conducted over two years in a snakebite-endemic region's tertiary care hospital, the retrospective analysis of patient data seeks to inform evidence-based treatment protocols and enhance management strategies in resource-limited settings, addressing a critical gap in current knowledge.

Aim and Objective

The primary goals of this study were as follows:

- Investigate the clinical manifestations, severity, treatment, and outcomes of snakebite patients at NCH SURAT.
- Examine the potential correlation between the timing of anti-snake venom (ASV) administration and the occurrence of complications due to delayed hospital arrival.

Through these objectives, the study aimed to enhance our understanding of factors influencing the prognosis and management of snakebites, particularly in cases where patients face delays in reaching the hospital.

2. Material and Methods

The study, conducted between June 2011 and November 2013 at New Civil Hospital Surat, focused on 100 adult snakebite cases meeting inclusion criteria (age >13 years, both sexes, and a confirmed history of snakebite). Cases with suspected bites from non-snake sources were excluded. Detailed patient histories were obtained, covering occupation, bite details, delay in seeking medical attention, and bite location. Physical examinations included general and local assessments, while severity was gauged using the modified Snake Bite Severity Score. All patients received ASV promptly upon hospital arrival, and the time elapsed between the bite and ASV administration was recorded. Prospective monitoring for complications followed.

Investigations encompassed various medical tests to comprehensively evaluate patients, covering blood, coagulation, liver and kidney function, urine analysis, electrolyte levels, E.C.G., chest X-ray, and a 20-minute whole blood clotting time examination.

3. Result and Discussion

In the research conducted at New Civil Hospital in Surat between June 2011 and November 2013, 100 cases of snakebite were examined in the medical ward and MICU. The study revealed a higher incidence of snakebites in the age group of 21–30 years, constituting 37% of cases, aligning with findings by S.A.M. Kularutne et al. [17]. This age range corresponds to a period of increased outdoor activities. Males were more commonly affected, with a male-to-female ratio of 2.03:1, consistent with Ghosh R. et al.'s study [18,19], suggesting that the higher incidence in males may be attributed to their predominant engagement in outdoor work. Furthermore, 75% of patients resided in rural areas, reflecting the favorable snake habitat in such regions. This finding resonates with studies by Inamdar IF et al., emphasizing the higher prevalence of snakebites in rural populations due to environmental factors and limited health education, as opposed to urban areas with less favorable conditions for snakes.[19]

Table 2 Patient demographic details

Parameter	Number	Percentage
Age group		
13-20	16	16
21-30	37	37
31-40	21	21
41-50	16	16
>51	10	10
Snake Bite and Gender		
Male	67	67
Female	33	33
Residential Area		
Rural	75	75
Urban	25	25

Table 2 indicates that there was no statistically significant difference in snakebite occurrence between day and night in the current study; however, night-time incidents, were more prevalent, constituting 52% of bites compared to 48% during the day. This finding aligns with Sharma SK et al.'s [20] previous research, which reported a majority of snakebites occurring at night. The increased incidence during nighttime is attributed to factors such as the absence of electricity and street lighting in rural areas, especially during the rainy season when snakes are active on the ground and farmers work in fields at night. Additionally, snakes exhibit nocturnal behavior and may enter human dwellings in search of food, a phenomenon more common in rural areas with abundant mice and rats. The cultural practice of sleeping on the floor in rural India heightens the risk of snakebites, as exposed body parts may be mistaken for prey by snakes.

The study analyzed the distribution of snakebite cases based on the month of admission, revealing that 79% of patients were admitted during the monsoon months (June to October), while only 4% were admitted during the winter months (January to March). This aligns with previous research by Sharma SK et al., indicating a higher incidence of snakebites during the monsoon season. The study attributes this increased incidence to the fact that snakes, being cold-blooded, are more active during the warmer months. Moreover, water entering snake burrows during the rainy season forces snakes out, leading to heightened exposure to humans, particularly in rural areas where farming activities increase the risk.[20]

Table 3 Clinical Presentation of Snakebite in the sample

Parameter	Number	Percent
Day-night distribution		
Day	48	48
Night	52	52
Clinical Presentation of Snakebite poisoning		
Neurotoxic	54	54
Hematotoxic	16	16
Neurotoxic + Hematotoxic	17	17
Local	7	7
Neurotoxic + ARF	2	2
Neurotoxic + Hematotoxic + ARF	1	1
Hematotoxic + ARF	1	1
Acute Renal Failure	2	2

Regarding bite sites, 64% of patients were bitten in the lower limb, consistent with Sharma SK et al.'s findings that 79% of snake bites occurred in the lower limb. This may be attributed to the prevalence of snakes on the ground, coupled with farmers often working barefoot. The study emphasizes the significance of timely hospital admission, with 60% of patients admitted within 6 hours and 12.7% admitted after 24 hours. Delayed admission resulted in increased morbidity and mortality, underscoring the importance of early medical management.[21]

Neurotoxic features were observed in 54% of patients, hematotoxic features in 16%, and both neurotoxicity and hematotoxicity in 17%. Local manifestations included pain (93%) and swelling (91%), with bleeding and cellulitis in 26% and 2%, respectively. Neurotoxic manifestations included ptosis (85%), blurring of vision (38%), difficulty breathing (30%), dysphagia, and diplopia. Hematotoxic manifestations showed 89% with prolonged prothrombin time, 80% with thrombocytopenia, and 74% with bleeding from the bite site. The study emphasizes the consistency of these manifestations with previous research, highlighting their importance in diagnosis and management.

The severity of snakebites was assessed using the Snake Bite Severity Score, revealing that higher severity grades were associated with delayed admission and significant mortality. The Chi-Square test indicated a significant association between the time lapsed before admission and snake bite severity grade. Patients admitted after 12 hours had higher severity scores, poorer outcomes, and more complications. The study underscores the critical role of early anti-snake venom (ASV) administration, with 76 patients receiving ASV within 12 hours and only one mortality, compared to 24 patients receiving late ASV, resulting in nine deaths.

The study's observation underscores the critical importance of timely availability and administration of anti-snake venom (ASV) in mitigating the risk of mortality and poor outcomes. The duration between venom injection and neutralization by ASV significantly influences the severity and outcome of envenomation. Early ASV administration is crucial in preventing complications and reducing the associated morbidity of systemic envenomation. This finding aligns with similar observations made by Vijeth SR et al. [22] and K Narvencar et al. [23], emphasizing the beneficial effects of prompt ASV administration in preventing adverse outcomes in patients with snakebites.

Table 4 Correlation of time with different parameters

Time (Hours)		**0 to 6**	**6 to 12**	**12 to 24**	**>24**
Time interval between bite and admission		60	16	17	7
Correlation of time interval between snake bite and time of admission and mortality		0	6.25	23.52	71.42
Correlation between time lapsed before admission snake bite severity grade	Grade 0	16	3	1	0
	Grade 1	35	8	3	2
	Grade 2	6	2	3	1
	Grade 3	3	3	6	1
	Grade 4	0	0	4	3
Correlation between bite to needle time and outcome	Survived	60	15	13	2
	Expired	0	1	4	5

4. Conclusion

In conclusion, the study conducted at New Civil Hospital in Surat provided valuable insights into venomous snakebites, shedding light on demographic patterns, clinical manifestations, and outcomes. The findings underscore the significance of factors such as age, gender, residential location, and timing of snakebite incidents. Notably, the study highlighted the prevalence of neurotoxic symptoms, emphasizing the importance of prompt recognition and treatment. The absence of fang marks in a significant percentage of cases and the efficacy of clinical severity scoring systems contribute to our understanding of snakebite management. Early intervention, particularly in administering antivenom, emerged as a crucial factor in mitigating complications and improving patient outcomes. The study's implications extend to healthcare practices, emphasizing the need for heightened awareness, early admission, and tailored interventions to address the diverse clinical presentations of venomous snakebites.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethics approval was granted by the Human Research Ethics Committee (HREC) of the Govt. Medical College, Approval No.MCS/STU/Ethics Approval/21414/2011.

Statement of informed consent

Participants are willing to participate in the study were included in the study.

Authors' contributions

All authors have equally contributed to the article.

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